

CLAIMS

What is claimed is:

1. An isolated polypeptide having the amino acid sequence X-Y-Z, wherein
X is a polypeptide having the amino acid sequence, or portion thereof, comprising
the amino acid sequence of a glycosylated interferon-beta;
Y is an optional linker moiety; and
Z is a polypeptide comprising at least a portion of a polypeptide other than
glycosylated interferon-beta.
2. The isolated polypeptide of claim 1, wherein X is interferon-beta-1a.
3. The isolated polypeptide of claim 1, wherein X is a mutant having at least one of
the following properties: (a) the mutant has a higher antiviral activity than wild
type interferon beta 1a, wherein the antiviral activity is measured by viral induced
lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater
antiviral activity than antiproliferative activity; (c) the mutant binds interferon
receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral
activity and lowered antiproliferative activity relative to its receptor binding
activity.
4. The isolated polypeptide of claim 2, wherein the interferon beta-1a is derivatized.
5. The isolated polypeptide of claim 4, wherein the derivative is a polyalkylglycol
polymer.
6. The isolated polypeptide of claim 1, wherein Z is at least a portion of a constant
region
of an immunoglobulin.
7. The isolated polypeptide of claim 6, wherein said at least a portion of the constant
region is derived from an immunoglobulin of the class selected from classes IgM,
IgG, IgD, IgA, and IgE.
8. The isolated polypeptide of claim 7, wherein the class is IgG.
9. The isolated polypeptide of claim 6, wherein the at least a portion of the constant
region comprises at least a hinge, CH2 and CH3 domains.
10. A fusion protein having an amino terminal region consisting of the amino acid
sequence of a glycosylated interferon-beta or a portion thereof and having a

carboxy terminal region comprising at least a portion of a protein other than glycosylated interferon-beta.

11. The isolated protein of claim 10, wherein X is interferon-beta-1a.
12. The isolated protein of claim 10, wherein X is a mutant having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type inteferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to its receptor binding activity.
13. The isolated protein of claim 11, wherein the interferon-beta-1a is derivatized.
14. The isolated protein of claim 13, wherein the derivative is a polyalkylglycol polymer.
15. The isolated protein of claim 10, wherein the at least a portion of the protein other than interferon beta is at least a portion of a constant region of an immunoglobulin.
16. The isolated protein of claim 15, wherein said at least a portion of the constant region is derived from an immunoglobulin of the class selected from classes IgM, IgG, IgD, IgA, and IgE.
17. The isolated protein of claim 16, wherein the class is IgG.
18. The isolated protein of claim 15, wherein the at least a portion of the constant region is comprises at least a hinge, CH2 and CH3 domains.
19. An isolated DNA sequence encoding for the protein of claims 1 and 10.
20. A recombinant DNA comprising the DNA sequence of claim 19 and an expression control sequence, wherein the expression control sequence is operatively linked to the DNA.
21. A host cell transformed with the recombinant DNA sequence of claim 20.
22. A method of producing a recombinant polypeptide comprising:
 - (a) providing a population of host cells according to claim 21; (b) growing said population of cells under conditions whereby the polypeptide encoded by said recombinant DNA is expressed; and (c) isolating the expressed polypeptide.

-62-

23. An interferon-beta fusion protein comprising a glycosylated interferon beta and additional polypeptide with which it is not natively associated, in substantially purified form
24. The fusion protein of claim 23, wherein said interferon beta is human interferon-beta-1a.
25. The fusion protein of claim 24, wherein said fusion has an antiviral activity that is selected from the group consisting of: (a) a higher antiviral activity than wild type interferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells, (b) a greater antiviral activity than antiproliferative activity, relative to wild type interferon-beta-1a, (c) an activity that includes receptor binding activity but, compared to wild type interferon-beta-1a, a lowered antiviral activity and lowered antiproliferative activity relative to said receptor binding activity.
26. A pharmaceutical composition comprising a therapeutically effective amount of the interferon beta fusion protein of claims 1, 10 and 23.
27. A method of inhibiting angiogenesis in a subject, comprising administering to a subject an effective amount of the composition of claim 26.
28. The isolated polypeptide of claim 3, wherein the mutant is derivatized.
29. The isolated polypeptide of claim 27, wherein the derivative is a polyalkylglycol polymer.
30. The isolated protein of claim 12, wherein the mutant is derivatized.
31. The isolated protein of claim 29, wherein the derivative is a polyalkylglycol polymer.

add a4